

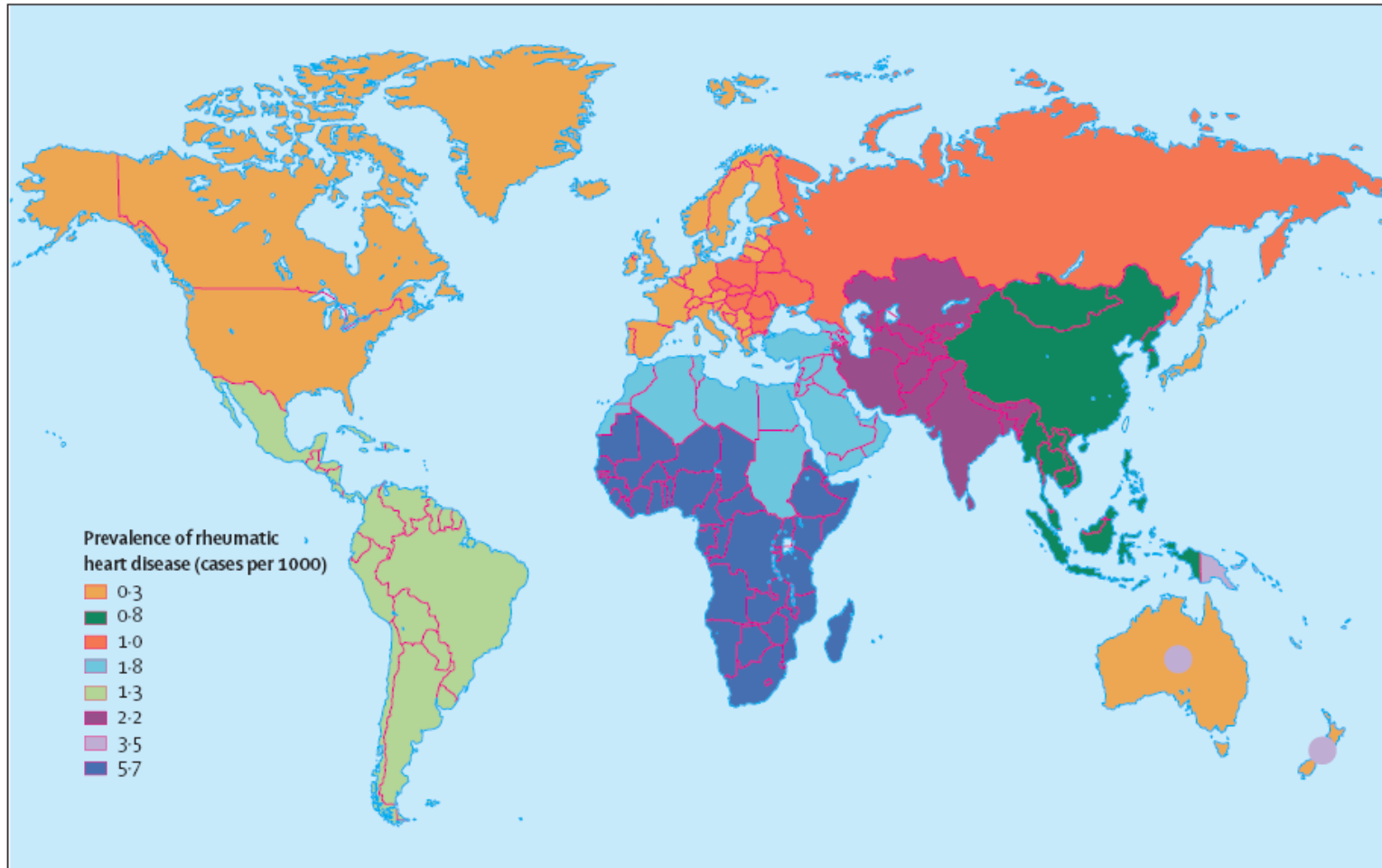
# Genetics of Rheumatic Heart Disease

The RHDGen Network

# Outline

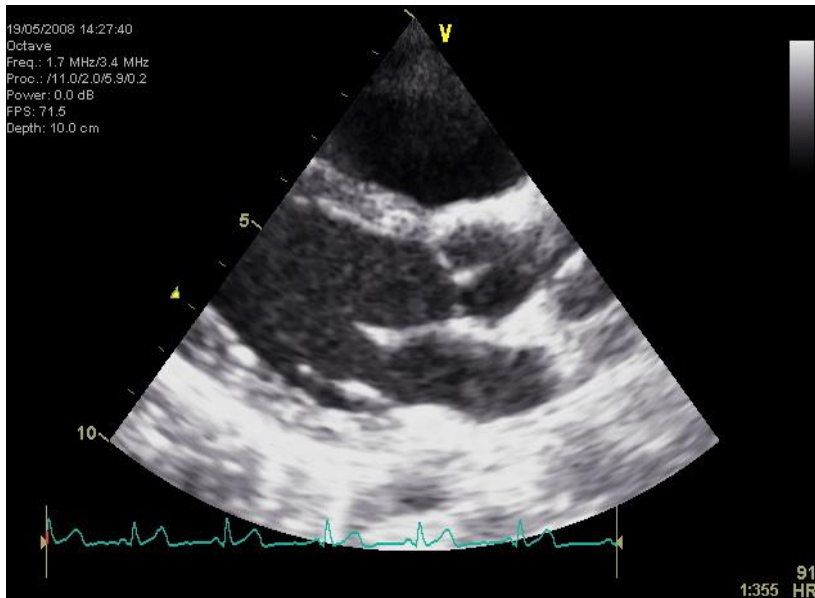
- Rationalé
- Proposed Activities
- Key Goals
- Organisation

# Global Burden of RHD



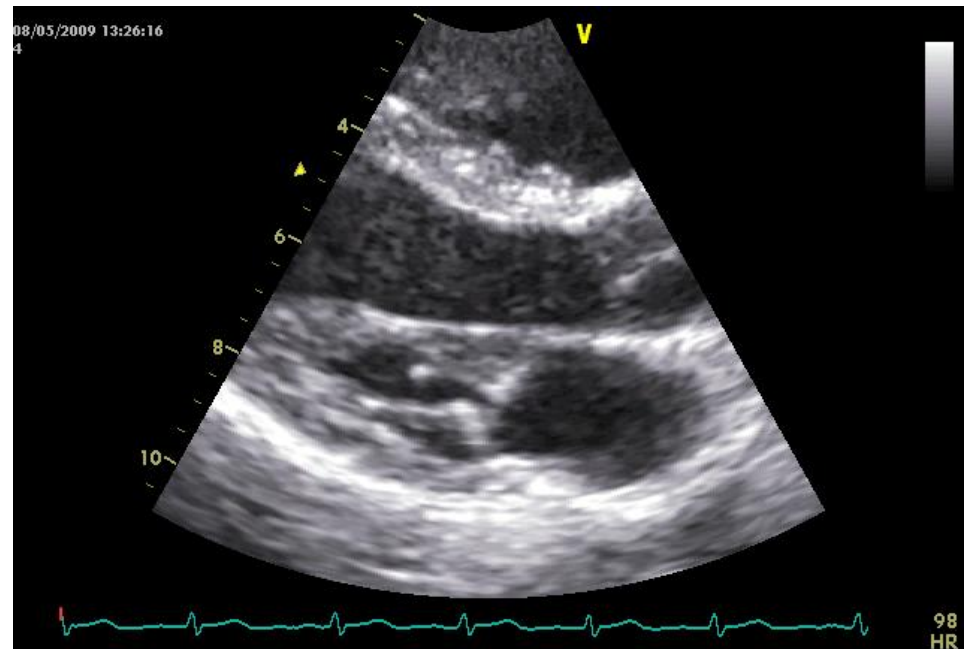
**Figure 1:** Prevalence of rheumatic heart disease in children aged 5–14 years

The circles within Australia and New Zealand represent indigenous populations (and also Pacific Islanders in New Zealand).



During an episode of ARF, valve changes can be minor and are still able to regress.

After recurrent episodes of ARF, thickening of subvalvar apparatus, chordal thickening and shortening and progression to permanent valve damage is evident.



# Pathogenesis

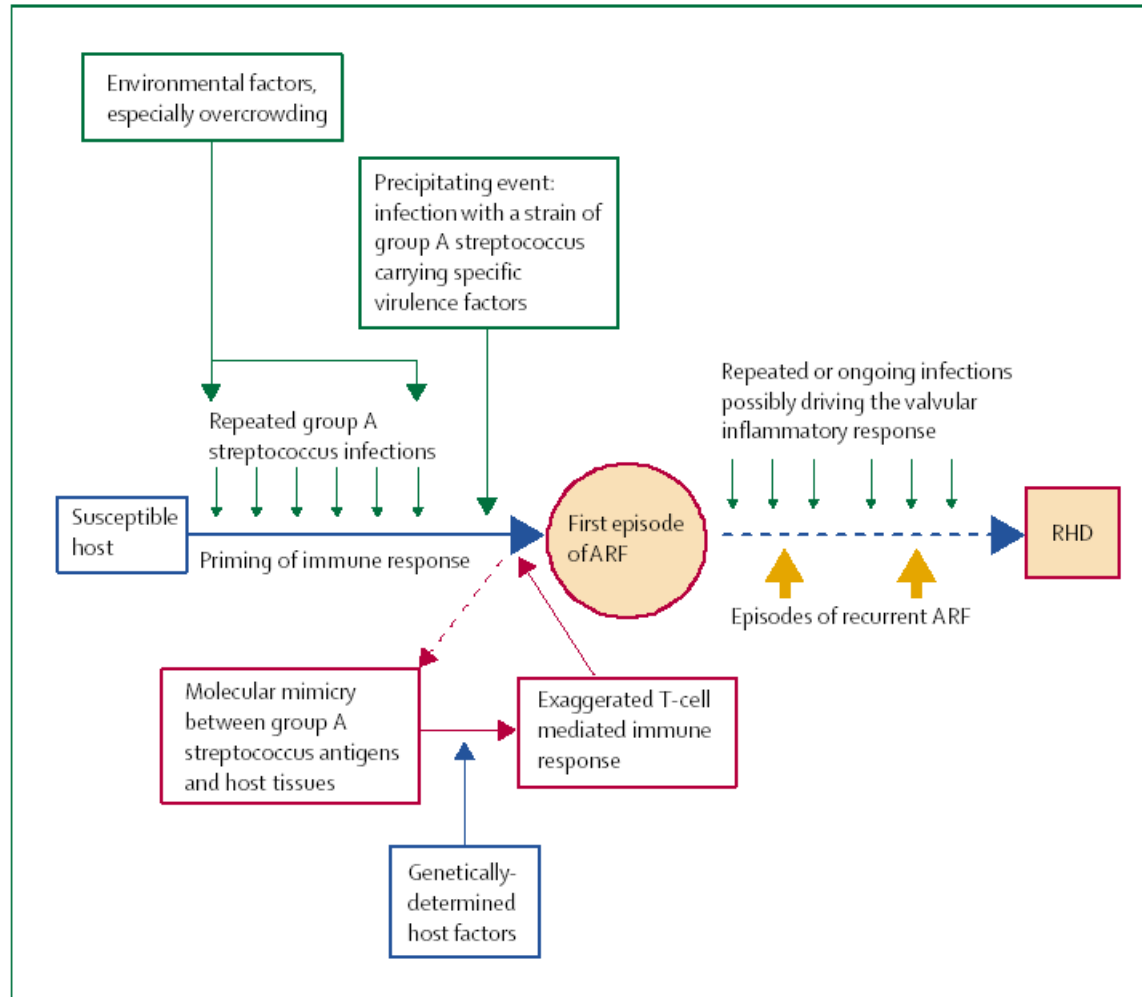
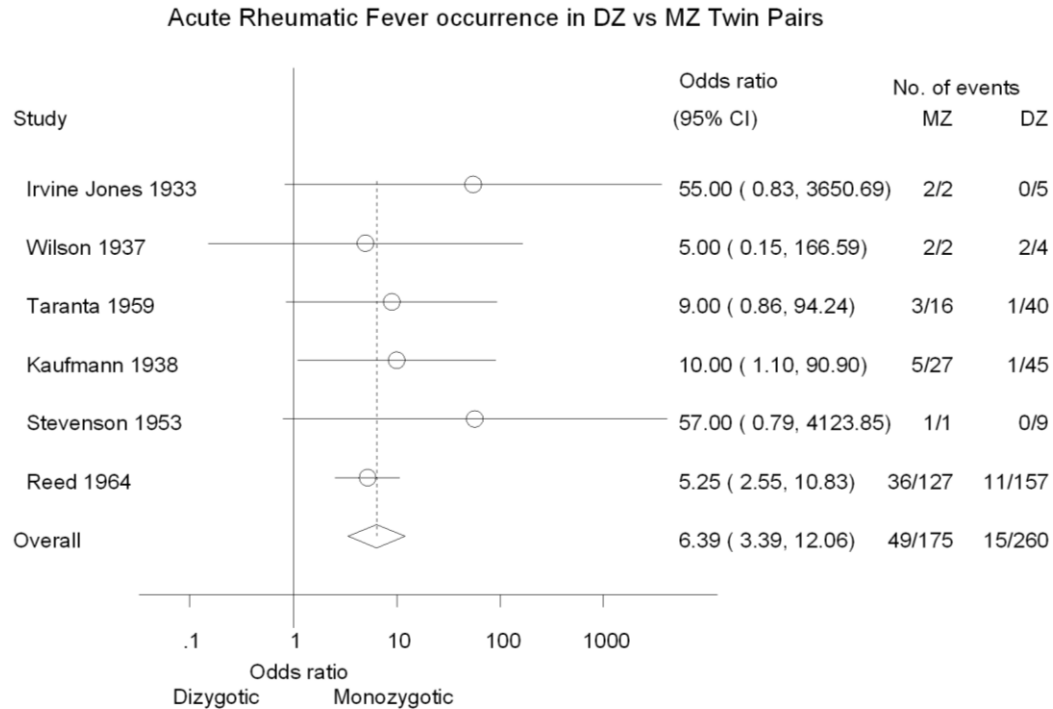


Figure 2: Pathogenetic pathway for ARF and RHD

# Heritability



**Figure 3.2.** Odds ratio of concordance for acute rheumatic fever according to type of zygosity

*Horizontal lines, 95% confidence interval; CI, Confidence interval; MZ, monozygotic; DZ, dizygotic*

# Activities of RHDGen

- To build a clinical and laboratory network for the phenotyping of RHD
- To identify genetic variants affecting susceptibility and resistance to RHD;
- To train a group of scientists and clinicians in genomic studies of multifactorial disease;
- To address ethical, legal, and social issues that are relevant to Africa

# Key Goals

- To recruit 2,500 patients with echocardiographically-confirmed RHD and 3,500 controls (1,500 unrelated; 2,000 family-based) from 8 sub-Saharan African countries,
- To conduct a case-control GWAS by genotyping 5 million SNPs in 1,500 RHD cases and 1,500 controls, followed by replication in 1,000 trios plus further genotyping and potentially sequencing loci of interest to identify causal variants.
- To train 16 scientists and clinicians in genomics at masters, doctoral and postdoctoral levels.



# Global Rheumatic Heart Disease Registry: The **REMEDY** study

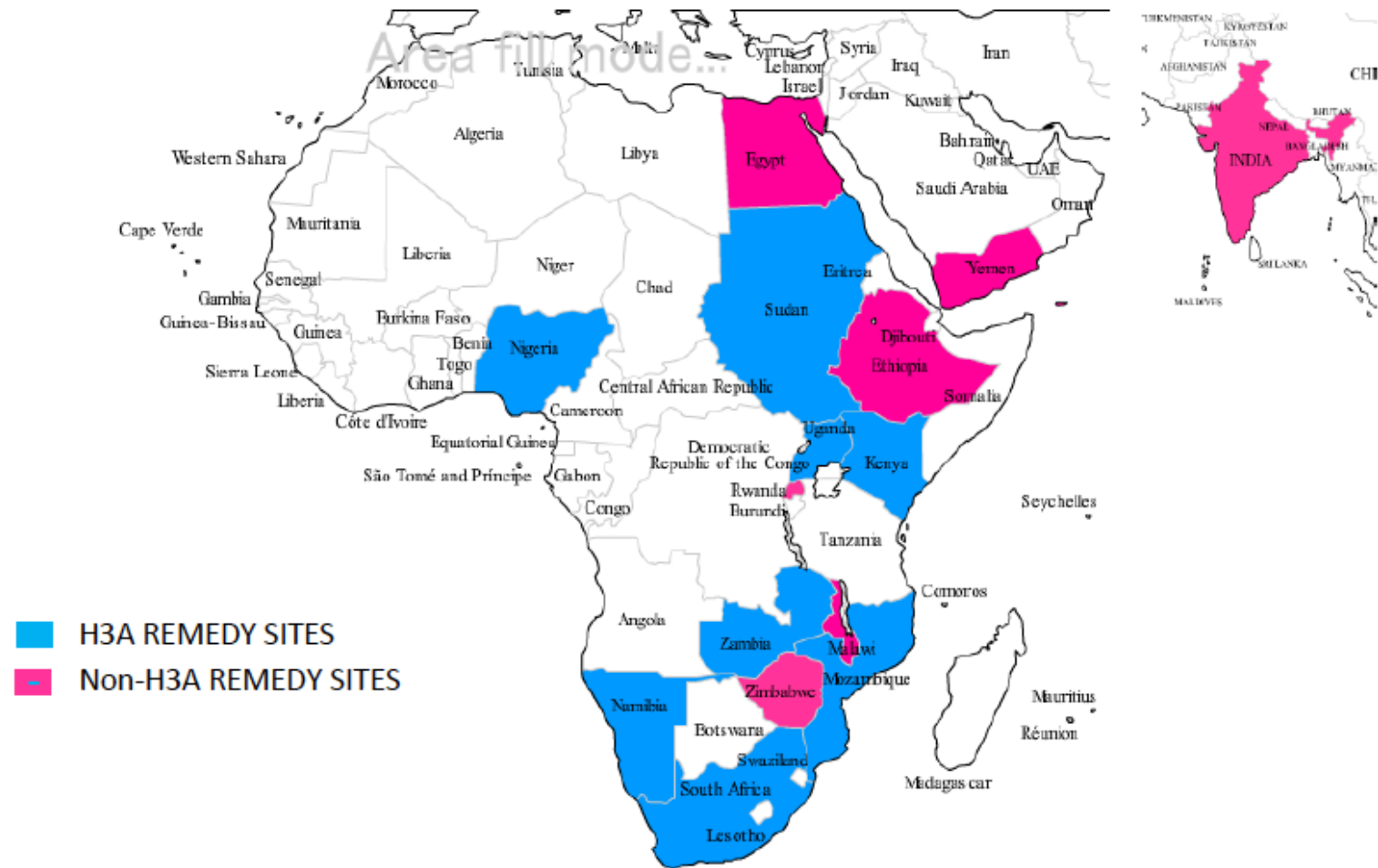
Figure 1



Countries participating in the vanguard phase of REMEDY individual sites, and their investigators are listed in the online [Appendix](#).

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# The Network



Appendix: The map shows in colour the 15 African and non-African countries with collaborative centres in the REMEDY study. The blue countries are participating in the RHDGen Network, and the pink countries are not participants in the RHDGen Network.

# Study Design of the GWAS

- **Discovery Cohort:**  
Case-Control genetic-association study of 1,500 RHD cases and 1,500 controls
- **Replication Cohort:**  
Family-Based association study of 1,000 probands + 2,000 parents
- **Combined Cohort:**  
Case-Control study of 2,500 cases and 2,500 controls/pseudo controls to identify further variants of modest effect

# RHDGen Health Scholars' Programme

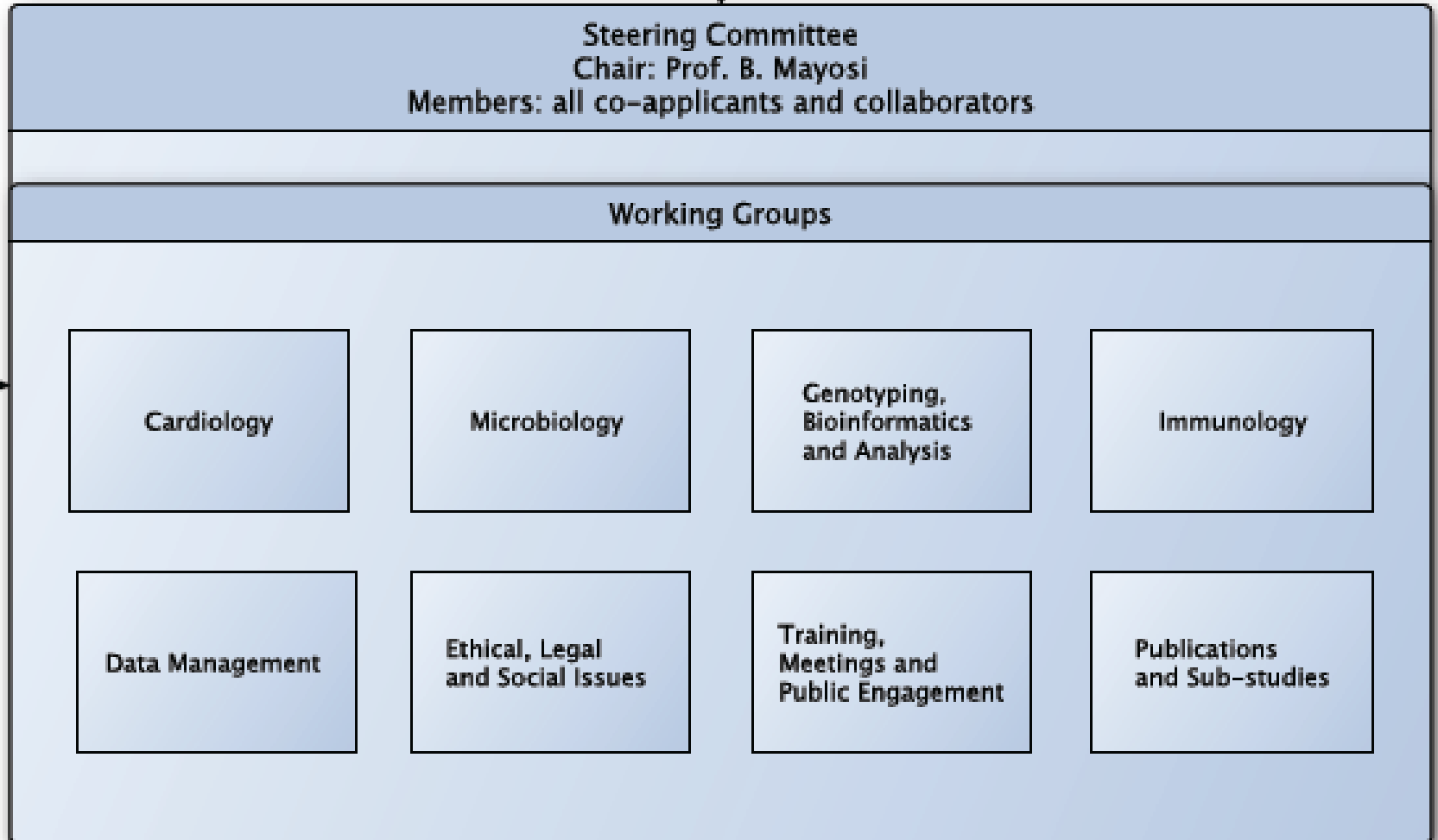
- Postdoctoral studentship in clinical science (n=1),
- PhD studentships in molecular genetics (n=1), bioinformatics (n 1), and statistical genetics (n=1),
- Masters studentships in bioethics (n=4),
- Master of Medicine (MMed) clinical studentships for trainees (registrars/clinical specialist trainees) at each contributing center (n=8).
- All the studentships will be advertised at the beginning of the programme and will be available on a competitive basis to students located in the institutions of the network.

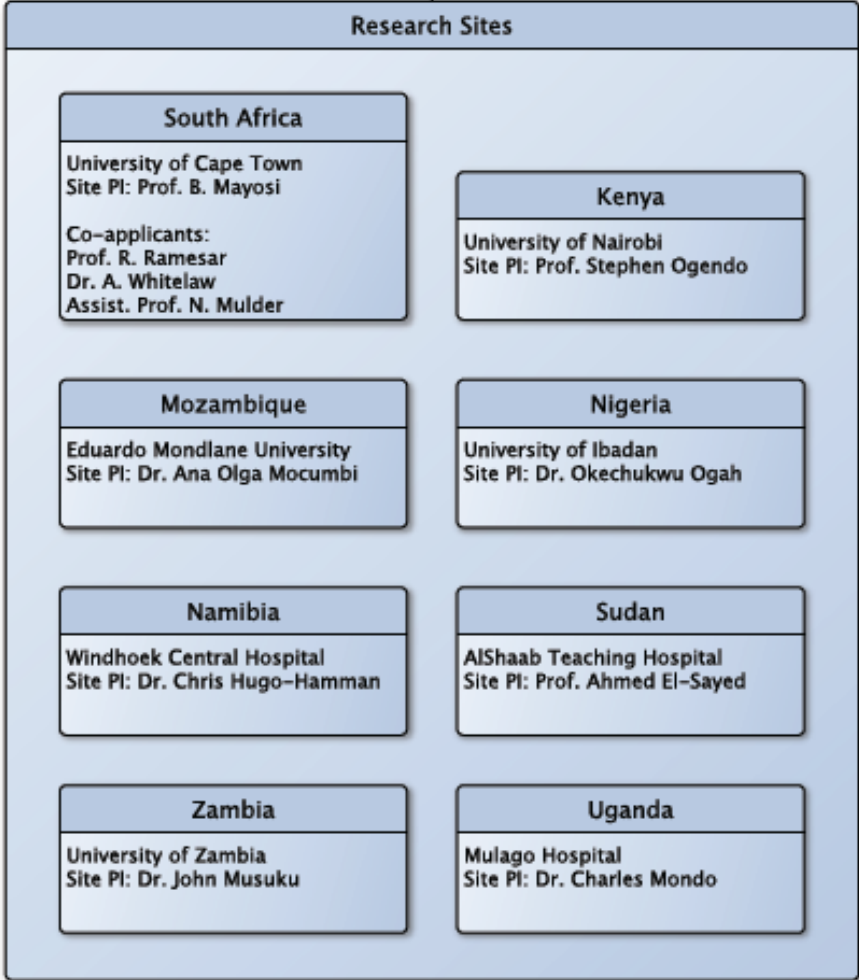
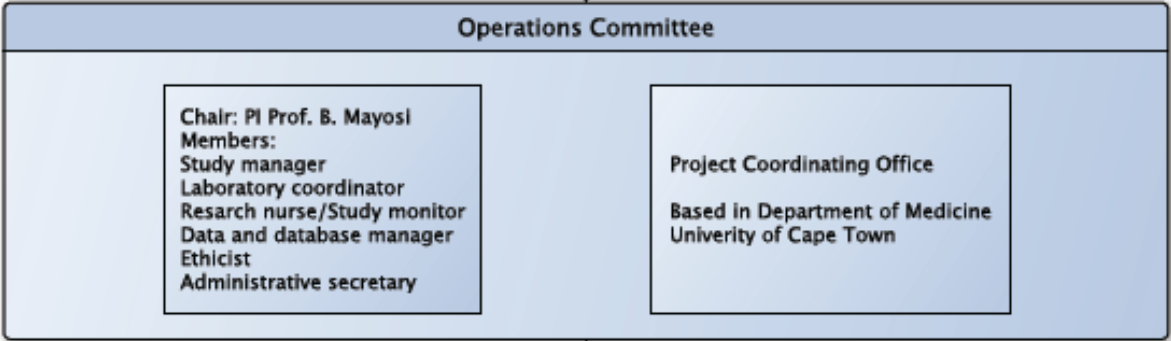
# ELSI

- Project ethicist embedded within the RHDGen project
- Four bioethics MSc students based at UCT
- Generate modules in ethics of genomics research in Africa
- Provide opportunity for network researchers to identify and discuss ethical issues in the consortium

# Organisation

**Scientific Advisory Committee**  
6 members; one from each continent with RHD endemic







## Collaborators

### Brazil

University of Sao Paolo  
Prof. L. Guilherme

### Canada

Population Health Research Institute  
University of McMaster  
Dr. G. Pare

### South Africa

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Hatter Institute for Cardiovascular Research  
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Biostatistics Research Unit  
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